Resources and Signaling in Multicellular Models of Plant Development

Henrik Jönsson
Division of Biology
California Institute of Technology
1200 E California Blvd.
Pasadena, 91125 CA
henrik@caltech.edu

Eric Mjolsness
Division of Biology
California Institute of Technology
1200 E California Blvd.
Pasadena, 91125 CA
emj@caltech.edu

Bruce E. Shapiro
Jet Propulsion Laboratory
California Institute of Technology
Pasadena, 91109-8099 CA
bshapiro@jpl.nasa.gov

ABSTRACT

The shoot apical meristem (SAM) of plants is the biological target for a mathematical model of multicellular organisms. The model is implemented in a computer program, and simulations of the dynamical time development are performed.

In plants, the shoot apical meristem is the source of the complete aboveground part of the organism. It retains a constant size and shape throughout the life of the plant, and it contains a regular dynamical pattern within itself. Arabidopsis has become somewhat of a model for plants [5, 7], and it has a SAM constituted of about 10^3 cells in an almost half spherical shape. It can be cytologically divided into zones [8], where the central zone is at the very apex, the periferial zone is on the sides, and the rib meristem is in the central parts of the meristem. It is known that the cell profileration rates are different in the different regions. In recent years, measurements of expression patterns of genes important for the phenotype have refined the regions of different cell types in the SAM (se e.g. [1]). Also the phenotype and expression pattern of mutants are used to find the roles of different genes in the development of the SAM. For example the clavata3 gene is thought to be a stem cell "marker", and the domain in which it is expressed is partly regulated by the clavata1/2 and wuschel genes [2, 1].

Another interesting developmental dynamic in the SAM, is the placement of new leaf and flower primordia. These are developed from the periferal zone, and the angular pattern of the positions are higly regular. The first two leaves are formed almost opposite from each other and then the leaves are formed in a spiralic pattern with an angle close to the golden angle (137.5 deg) between consecutive primordia. Both e.g. the pin-formed1 gene and the hormone auxin is known to play an intrinsic role in the formation of the new primordia [10, 12].

To obtain these stable regular patterns a complex interaction network between proteins and hormones must be present. These interaction also must reach intercellular levels. Although parts of these interactions are known, most are yet to be discovered, and a mathematical model of the interactions is a helpful tool to produce hypothesis and check behavior of the regulating networks. Here we extend a multicellular model [11, 9] to incorporate a more thorough description of intercellular signaling.

The basic mathematical model is described in [11]. The cell shapes are approximated as spheres and the cell growth is radially symmetric. A mechanical interaction between cells is described by a spring potential between each pair of cells with a relaxing distance equal to the sum of the radii. The interaction is softly truncated for larger distances, such that there is no mechanical interaction between cells further apart from each other than a threshold value. At a cell division the total mass is conserved. At the first step of the division, two smaller spheres are created and placed partly on top of each other and then the action of the spring force moves the new cells apart.

Proteins are implemented by concentration values in each cell, and the dynamics are described by a neural-network inspired genetic regulatory network (grn) model [6]

$$\tau_a \dot{v}_a^{(i)} = g(u_a^{(i)} + h_a) - \lambda_a v_a^{(i)},$$

where

$$\begin{aligned} u_a^{(i)} &= \sum_b T_{ab} v_b^{(i)} + \sum_j \Lambda_{ij} \left(\hat{T}_{ab} v_b^{(j)} + \sum_{bc} \tilde{T}_{ac}^{(1)} \tilde{T}_{cb}^{(2)} v_b^{(j)} v_c^{(i)} \right) \\ g(x) &= \frac{1}{2} \left(1 + \frac{x}{\sqrt{1+x^2}} \right). \end{aligned}$$

In the equations the v's are the protein concentrations, a, b are indeces for the proteins and i, j are indeces for the cells. The model describes intracellular interactions between proteins (encoded by the T matrix), as well as intercellular interactions between proteins of neighboring cells. The intercellular part contains a direct interaction ($\hat{T}$), and also a ligand-receptor type of interaction ($\tilde{T}^{(1)}\tilde{T}^{(2)}$). The λ term is a degradation term, τ is a time parameter, and h is a parameter regulating the default expression. Λ describes the connection between cells. Different cell types have different protein concentrations and this is used to affect e.g. the growth and cell cycle periods as described below.

Resources and signaling molecules are implemented much in the same mathematical form, using concentration values, R, for each cell. The differential equations are

$$\dot{R}_b^{(i)} = k_b^{(i)} + \alpha_b \sum_j G_{ij}(R_b^{(j)} - R_b^{(i)}) - \beta_b R_b^{(i)} - \gamma_b \dot{M}^{(i)} + \delta_b \dot{R}_{b,(transport)}^{(i)}.$$

Here b is a resource index and i, j are cell indeces. The creation (k term) can be restricted to specific cells which may reflect a transport from outside the simulated region. There is also a degradation term (β), and if applicable a loss of resource due to the growth of a cell (γ). Apart from these terms the total amount is constant for the organism, and the compounds can be transported between neighboring cells by diffusion (α) and/or by active transport (δ). The G describes the connections between cells. Using these mechanisms, patterns in the resource concentrations can be produced in the simulated organism, leading to different cell behavior as described below.

The cell growth is proportional to the mass of the cell, and the proportionality factor is a function of both the protein concentrations and resource concentrations in the cell. The protein concentration part is a sigmoidal function, and the resource part is a threshold function which is linear for small concentrations and has an upper limit for a maximum concentration.

Different models for the cell-cycle can be used. The simplest implementation uses only the cell size, and the cells divide when the mass reaches a threshold value. A more biologically interesting implementation uses the Goldbeter model [4], and the period can be tuned by a binding of proteins or resource/signaling molecules described above to the cycline protein as proposed in [3]. Using this model, the growth is decoupled from the proliferation of the cells.

In our simulations we show how the described model can be used to simulate qualitative behavior of the SAM in plants.

Dynamical regions with different gene expressions are simulated where the regions increase size by cell growth/division and decrease size by differentiation into other cell types. This is all modeled using the grn-protein model and the simulations also shows the need of resources/signaling for the stability of the system. The simulation produces a SAM where the central zone cells change state into periferal zone or rib meristem cells and these are later changing into cells of the stem (no primordia are simulated). The cell fate is determined by the neighborhood, which is highly probable behavior in the SAM.

In another simulation a signaling molecule is used to create patterns of concentrations resembling the phyllotactic pattern in the outer cell layer of the SAM. The molecule could be interpreted as auxin which, as described earlier, is important for the formation of primordia.

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